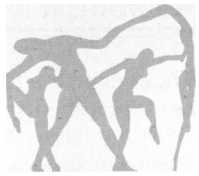

Women and Medicine

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Diagnostic and Treatment Challenges

JENNIFER H. WEAR, MD, *Contributing Editor*

Recurrent Urinary Tract Infections

OF THE MANY gynecologic and hormonal health problems that cause women discomfort and concern, none is more easily managed than recurrent urinary tract infections. Of all recurrences, 99% or more are reinfections—that is, each infection is caused by a new and different organism from the rectal reservoir of bacteria. Recognition of this reservoir, and the fact that each infecting strain must first colonize the vaginal mucosa before it enters the bladder, has major consequences for both diagnosis and treatment.

To accurately diagnose the presence of bacteria in the bladder urine, contaminating pathogenic organisms on the vaginal and urethral mucosa must be avoided. This task is accomplished most accurately by doing a suprapubic needle aspiration of a full bladder, almost as accurately by catheterizing the bladder—the bladder must be full and the specimen for culture collected only after several hundred milliliters of urine have washed out the contaminating urethral bacteria—and much less accurately by separating the patient's labia and collecting, under direct vision, a late voided specimen from a full bladder. With the first two techniques, the presence of any number of bacteria is diagnostic of an infection; with the last technique, 1,000 or more bacteria per milliliter should indicate an infection within the bladder. The presence of many leukocytes per high-power field in a centrifuged urine aliquot can be confirmatory.

Colonization of the vaginal mucosa by rectal bacteria has equally major consequences for treatment. There are several effective regimens, all of which depend on the biologic principle that an oral antimicrobial agent must not carry a high risk of altering the lower rectal bacterial reservoir and especially should not induce resistance. The most useful agents are trimethoprim-sulfamethoxazole, nitrofurantoin, cephalexin, and cinoxacin, all used in prophylactic dosages of a quarter to half of a standard-sized tablet. The smaller the dose, the less the adverse effect on the rectal reservoir. Successful prophylactic strategies include a single, small, postintercourse dosage for sexually active women, including—at least for nitrofurantoin and cephalexin—reinfections during pregnancy; nightly bedtime prophylaxis for very sexually active women; and even thrice-a-week bedtime prophylaxis. All of these work well. A fourth, and very effective, nonprophylactic regimen is to wait and treat each infection at the first sign of recurrent symptoms; full-dosage therapy for three days is more than adequate with any of these four drugs. For a patient who has three or fewer infections per year, this fourth regimen is the most desirable and acceptable to women. They must be allowed, however, to have the antibacterial agent on hand and to institute their own therapy without benefit of an office visit; if their symptoms persist for longer than five or six days, an office visit is appropriate. For a sexually active woman with more than three infections per year, postintercourse prophylaxis is the most effective with the least amount of drug. For a woman or child with reinfections who is not sexually active, bedtime prophylaxis on a nightly or thrice-a-week regimen is usually required.

Before considering those rare cases of women who have more serious infections, physicians should remember that a diagnosis of urinary tract infection cannot be established by symptoms alone; indeed, 27% to 34% of women thought to have acute cystitis will have sterile urine on urethral catheterization—the so-called urethral syndrome about which so little is known—but vaginitis caused by *Candida* or *Trichomonas* should also be ruled out by examining under a microscope a wet vaginal smear. It should also be recognized that pyuria—five or more leukocytes per high-power field in a centrifuged specimen—occurs in only 50% of asymptomatic women with a urinary tract infection, and that pyuria can occur without infections in several diseases of the urinary tract such as interstitial cystitis and in situ carcinoma of the bladder. Thus, it is difficult to rely exclusively on urinalysis for the diagnosis of urinary tract infection. Interestingly, however, there is no solid evidence that asymptomatic urinary tract infections need to be treated except during childhood and pregnancy. There is clearly no reason to treat asymptomatic infections in the elderly or in patients with an indwelling urethral catheter. If symptoms occur in a catheterized patient, especially fever, therapy for a few days is warranted, but continuous antimicrobial treatment is wasted and simply insures infection with multiply resistant bacteria.

Most female patients with recurrent pyelonephritis, including children younger than 2 years, also have ascending reinfections of their urinary tract; they should probably be treated for seven to ten days rather than the three-day regimen described above for recurrent cystitis. To be sure, a few female patients with recurrent infections are at an increased risk of renal damage or at least severe morbidity, and their cases should be recognized and treated with special care. These patients include children younger than 2 years with severe ureteral reflux (all recurrences are reinfections, however); women with recurrent *Proteus mirabilis* urinary infections in whom the urea-splitting bacteria have caused a struvite renal stone to form; women with renal papillary necrosis due to diabetes mellitus or analgesic abuse who may have high-pressure obstruction of their ureters, causing severe renal damage; women with spinal cord injury with an associ-

ated high-pressure obstruction of the bladder from pelvic floor spasms; women with diabetes who have chills, fever, flank pain, and emphysematous pyelonephritis (diagnosed by finding intraparenchymal or perirenal gas on a plain film of the abdomen), a disease that carries a 43% mortality without early diagnosis and surgical drainage; and, finally, women who have pyelonephritis in the last trimester of pregnancy, a condition easily prevented by the diagnosis of a urinary tract infection in the first trimester, treated for three days with curative oral antimicrobial therapy, and followed by post-intercourse prophylaxis with nitrofurantoin or cephalexin.

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Premenstrual Syndrome

ALTHOUGH IT WAS FIVE DECADES AGO that Frank first described the premenstrual syndrome in the medical literature, little progress has been made in our understanding of this condition. As a result, family, friends, and physicians have often rejected the idea that it is a medical disorder and accused women with premenstrual symptoms of a lack of character, sanity, or moral fiber. This situation is not surprising, however, for until recently there has not been a clear definition or set of diagnostic criteria, a convincing theory for its etiology, or a proven approach to the therapy for the premenstrual syndrome.

Fortunately, a renewed interest in this phenomenon in the early 1980s by the medical and popular press has led to a serious attempt by many medical and social scientists to unravel the mysteries of this enigmatic problem. The first major article written by medical researchers in this country in the 1980s was by Reid and Yen.[1] They stated their belief that the premenstrual syndrome was a psychoneuroendocrine disorder—that is, a condition resulting from a disturbance of the neuroendocrinologic system but greatly influenced by psychosocial factors. Based on animal studies that showed a premenstrual decline in β-endorphins in the hypophyseal portal system and the similarity of many premenstrual symptoms to those that accompany an exposure to and withdrawal from narcotics, they proposed that a withdrawal from endogenous opiates may incite premenstrual symptoms. Unfortunately, studies of circulating endorphins in women with and without premenstrual symptoms proved contradictory. In the minds of many, however, their article legitimized the premenstrual syndrome as a medical disorder and stimulated the search for a common biochemical defect or a biological marker for the condition, a search that has not yet been successful.

While failure to discover a biochemical defect or biochemical marker has convinced some that the premenstrual syndrome is not a medical diagnosis at all, this failure probably reflects more our limited understanding of psychoneuroendocrinology and the limitations of our investigative tools and techniques than the nature of the syndrome.

Another problem facing clinicians and researchers had been the absence of a universally accepted set of diagnostic criteria. The 1980s, however, also produced a landmark article by Rubinow and Roy-Byrne that critically analyzed the methods of the past, established guidelines, and set standards for designing valid and reproducible studies.[2] Consequently, recent published studies of the premenstrual syndrome have been of higher quality and more believable than at any time in the past. As a result, many skeptical physicians are now taking an active interest in this issue. They recognize that distressing symptoms begin about 2 weeks before the menses and end within 24 hours after the menses begin. The most common physical symptoms are fatigue, headache, abdominal bloating, breast tenderness and swelling, and acne. Anxiety, hostility or anger, and depression occur in more than 94% of women with the syndrome. Many have psychological reactions such as guilt, decreased self-esteem, and shame; many also report notably disturbed family and work lives.

Another encouraging development has been the improved communication that has occurred between the psychologically oriented "camp" and the biologically oriented one of investigators and clinicians.[3] Whereas each camp previously gave lip service to the other, now each borrows concepts and methods from the other. Realizing that the premenstrual syndrome most likely is the result of both external (social) and internal (psychobiologic) factors, multidisciplinary teams have been formed to study, evaluate, and treat women with the disorder. This cooperation has led to new and effective treatment approaches, including various combinations of education, medication, and counseling—peer, individual, group, family, and marital. It now appears that a biopsychosocial model of the syndrome has come of age.[4]

Despite these dramatic advances in the field of "PMS-ology," we still have a long way to go. Scientists and health care providers, however, can be excited about the rapid rate at which insight into the nature of the syndrome is being gained. Most important, women with the disorder can be increasingly optimistic that in the future their care will be even more compassionate and effective.

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Advances in the Diagnosis and Treatment of Ovarian Cancer

OVARIAN CANCER is responsible for the death of more American women than cancers of the uterine cervix and corpus combined. It has been estimated that 19,000 new cases of ovarian cancer will be diagnosed in 1988 and that 12,000 of these women will eventually die of their disease.

Approximately 70% of all patients with epithelial ovarian cancer present with disease that has already spread beyond the confines of the pelvis to involve peritoneal sites throughout the abdomen. The role of aggressive cytoreductive surgery in the management of these patients remains